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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SZPERKA, MICHAEL EDWARD	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 03/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/690,639	DE SILANES ET AL.	
	Examiner	Art Unit	
	Yunsoo Kim	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30,31,36,44-57,61-63,67,68,71 and 74-76* is/are pending in the application.

4a) Of the above claim(s) *46-54 and 61-63* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30,31,36,44,45,55-57,67,68,71,74-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/20/04,3/4/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 30, 31, 36, 44-57, 61-63, 68, 71 and 74-76 are pending.

2. Applicant's election with traverse of Group I drawn to claims 30, 31, 36, 44, 45, 55-57, 67, 68, 71 and 74-76 is acknowledged in the reply filed on 1/6/06.

Applicants traverse the rejection based on the Group I cannot be made by any other materially different process and no serious search burden imposed for species.

This is not found persuasive because the pending claims of each group from the original restriction are patentably distinct. Antibody fragments can be produced by recombinant method (e.g.Fab express library methods) and as evidenced in p. 4-5 of specification, other means to purify antibody fragments can be employed. It is undue burden to search more than one invention. A prior art reads on an antibody to cytokines differs from a prior art reads on antibody to a venom of a scorpion. The requirement is still deemed proper and is therefore made FINAL.

Accordingly, claims 46-54 and 61-63 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected invention/species.

Currently, claims 30, 31, 36, 44, 45, 55-57, 67, 68, 71, 74-76 are under consideration.

3. Applicants' IDS filed on 8/20/04 and 3/4/05 have been acknowledged. However, AL1 is considered to the extent to the claim as applicants have not provided the English translation. In addition, AS5, the international search report, has been considered but crossed out as being inappropriate for IDS.

4. Applicant is required to update US priority in the first line of the specification and update status of all pending applications.

5. The specification stand objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: The phrase "a purified molecule" in claim 30 does not have the written support in the specification. Applicant is requested to identify the written support for the claimed limitation.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 30, 31, 36, 44, 45, 55-57, 67, 68, 71, 74-76 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising of a polyclonal antibody $F(ab')_2$ binds to an antigen; does not reasonably provide enablement for a pharmaceutical composition comprising of a polyclonal antibody $F(ab')_2$ binds to venom of scorpion and neutralizing venom. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and /or use the invention commensurate in scope with these claims.

The specification does not enable one of skill in the art to practice the invention as claimed without undue experimentation. Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed.Cir.1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of the skilled in the art to practice the claimed invention.

It is at issue whether or not the claimed invention would function as pharmaceutical composition. In view of absence of a specific and detailed in Applicants' specification of how to effectively use the pharmaceutical composition comprising the polyclonal antibody $F(ab')_2$ as claimed, and absence of working examples providing evidence which is reasonably predictive that the claimed pharmaceutical composition are effective for in vivo use, and the lack of predictability in the art at the time the inventions was made, an undue amount of experimentation would be required to

practice the claimed pharmaceutical composition with a reasonable expectation of success. Example 7, p. 23 of the instant application discloses in vivo experiment of venom of non-scorpion species.

The specification as filed does not provide a definition of "neutralizing a purified antigenic molecule" in addition to insufficient guidance and direction to the nature, parameter and endpoints of "neutralizing" the antigenic molecule.

While "neutralizing" encompasses a broad range of mechanisms or endpoints of rendering the molecule, applicants have not provided sufficient direction how to use antibodies that neutralize an antigenic molecule by any mechanisms (e.g. degrading the antigenic molecule versus blocking a specific activity). Reasonable correlation must exist between the scope of the claim and the scope of enablement set forth.

Burton et al. (Nature Immunology, 2004, vol. 5, No. 3, p. 233-236) mention the problems associated with neutralizing antibodies. Binding of a monoclonal antibody has to be specifically at the reactive sites. Specific binding anywhere else on the peptide does not elicit desired neutralization effect. The specification does not disclose whether the antibody would bind to specific reactive site of the antigenic molecule.

Vanlandschool et al. (J. General Virology, 1998, 79:1781-1791) describe a monoclonal antibody binds to the membrane proximal end of influenza virus haemagglutinin (H3 subtype) does not neutralize the virus. Different binding assays show that the monoclonal antibody binds to the polypeptide however due to inaccessibility of the epitope, the binding of the monoclonal antibody does not translate into neutralization of the virus.

Given the number of possibilities associated with neutralizing an antigenic molecule, including via direct or indirect effects associated with antigenic structure or function, as to whether such a desired effect can be achieved or predicted, as encompassed by the claim, it would take undue experimentation to practice the claimed invention.

To summarize, reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view or the quantity of experimentation necessary, the limited working example, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breath of the claims, it would take undue trials and errors to practice the claimed invention.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 30, 36, 44, 45, 55, 67, 68 and 76 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S.Pat. 4,849,352 (IDS reference) as evidenced by Harlow and Lane (Antibodies, 1988, Cold Spring Harbor Lab., p.298-199) and Campbell (Monoclonal and Immunosensor Technology, 1991, Elsevier, vol. 23, p. 288-291).

The '352 patent teaches a pharmaceutical composition comprising a polyclonal $F(ab')_2$ binds to any antigen, pepsin digested followed by ammonium sulfate precipitation (col 3, lines 22-41, col. 2, lines 51-65).

The '352 patent further teaches that the antibody fragments are quickly distributed in the body, filtered and excreted by the kidney. Toxin neutralization by antibody fragments and volume circulating are greater than IgG (col. 1-2 overlapping paragraph).

It is well known in the art as evidenced in Harlow and Lane (p. 299), repeating the precipitation process as necessary is within the optimization of procedures. Furthermore, the range of the first ammonium sulfate precipitation at about 16-22% and the second precipitation at about 32-38% is taught in Harlow and Lane as further evidenced by Campbell.

Campbell defines 100% saturated ammonium sulfate having 770g/l. Harlow and Lane suggest addition of 0.5 volume and to 50% saturation of saturated ammonium sulfate (step. 3, p. 299) to antibody solution which results 1.5 total volume. The final concentration of ammonium sulfate is ~250g/l, which is equivalent to 25% by weight.

The concentration range of the second ammonium sulfate precipitation is met by addition of ammonium sulfate to 50% saturation (step 4), having 770g/l, 50% saturation is equivalent to 385g/l, or 38.5% by weight.

The limitation " pharmaceutical" is met as the purified antibody after dialyzed against distilled water (e.g. pharmaceutically acceptable carrier, col. 8, lines 8-50) and 100ul of antibody injected to Swiss Webster mice (col. 11, lines 1-10). In addition, " substantially free of albumin, pyrogens and viral particles" is inherent property of any antibody purified by pepsin digestion and ammonium sulfate precipitation.

Claim 68 is included in this rejection due to the lack of definition of " neutralizing" while the prior art teaches antivenin activity (col. 2, lines 51-53). Thus, the reference teachings anticipate the claimed invention.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 30, 31, 36, 44, 45, 55-57, 67, 68, 71, 74-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S.Pat. No. 5,443,976 in view of U.S. Pat. No. 4,849,352 (IDS reference) as evidenced by Harlow and Lane (Antibodies, 1988, Cold Spring Harbor Lab., p.298-199) and Campbell (Monoclonal and Immunosensor Technology, 1991, Elsevier, vol. 23, p. 288-291).

The '976 patent teaches IgY polyclonal antibody to scorpion venom, *Centruroids noxius* (col. 11, lines 43, Example 52).

The '976 patent does not teach $F(ab')_2$ fragments by pepsin digestion and ammonium sulfate precipitation.

However, the teachings of the '352 patent as evidenced by Harlow and Lane and Campbell regarding F(ab')2 antibodies have been discussed, supra.

Therefore, one of the ordinary skill in the art would have been motivated to combine teachings of antibody to scorpion venom *Centruroids noxius* taught by the '976 patent in the teachings of the '352 patent to produce more readily utilizable antibody to scorpion venom. The '352 patent teaches intact IgG is too large to excreted by kidney functions and antibody fragments excrete many kinds of neurotoxins that are not accessible to IgG (col. 2, lines 22-50).

From the combined teachings of references, one of ordinary skill in art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of the ordinary skill in the art at the time the invention was made, as evidenced by references, especially in the absence of evidence to the contrary.

12. No claims are allowable.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yunsoo Kim whose telephone number is 571-272-3176. The examiner can normally be reached on Monday thru Friday 8:30 - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic
Business Center (EBC) at 866-217-9197 (toll-free).

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